Docket No.: PRD-0034

App No.: Not Yet Assigned Filed: Herewith

Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE

Inventors: Lovenberg et al. Attorney: Felicity E. Groth Sheet 1 of 13

Phone: (215) 568-3100

1/13

Figure 1: Nucleic Acid coding sequence human histamine H4

ATGCCAGATACTAATAGCACAATCAATTTATCACTAAGCACTCGTGTTACTTTAGCATTT TTTATGTCCTTAGTAGCTTTTGCTATAATGCTAGGAAATGCTTTGGTCATTTTAGCTTTTG ACTTCTTTGTGGGTGTGATCTCCATTCCTTTGTACATCCCTCACACGCTGTTCGAATGGG ATTTTGGAAAGGAAATCTGTGTATTTTGGCTCACTACTGACTATCTGTTATGTACAGCAT CTGTATATAACATTGTCCTCATCAGCTATGATCGATACCTGTCAGTCTCAAATGCTGTGT CTTATAGAACTCAACATACTGGGGTCTTGAAGATTGTTACTCTGATGGTGGCCGTTTGG GTGCTGGCCTTCTTAGTGAATGGGCCAATGATTCTAGTTTCAGAGTCTTGGAAGGATGA AGGTAGTGAATGTGAACCTGGATTTTTTTCGGAATGGTACATCCTTGCCATCACATCATT CTTCCAACATCTGTGGACACTCATTCAGAGGTAGACTATCTTCAAGGAGATCTCTTTCTG CATCGACAGAAGTTCCTGCATCCTTTCATTCAGAGAGACAGAGGAGAAAGAGTAGTCTC ATGTTTTCCTCAAGAACCAAGATGAATAGCAATACAATTGCTTCCAAAATGGGTTCCTT CTCCCAATCAGATTCTGTAGCTCTTCACCAAAGGGAACATGTTGAACTGCTTAGAGCCA GGAGATTAGCCAAGTCACTGGCCATTCTCTTAGGGGTTTTTGCTGTTTTGCTGGGCTCCAT ATTCTCTGTTCACAATTGTCCTTTCATTTTATTCCTCAGCAACAGGTCCTAAATCAGTTTG GTATAGAATTGCATTTTGGCTTCAGTGGTTCAATTCCTTTGTCAATCCTCTTTTGTATCCA TTGTGTCACAAGCGCTTTCAAAAGGCTTTCTTGAAAATATTTTGTATAAAAAAAGCAACC TCTACCATCACAACACAGTCGGTCAGTATCTTCTTAA

Docket No.: PRD-0034

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Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE
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Attorney: Felicity E. Groth Sheet 2 of 13 Phone: (215) 568-3100

2/13

Figure 2: Amino acid sequence human histamine H4 receptor

Met Pro Asp Thr Asn Ser Thr Ile Asn Leu Ser Leu Ser Thr Arg Val Thr Leu Ala Phe Phe Met Ser Leu Val Ala Phe Ala Ile Met Leu Gly Asn Ala Leu Val Ile Leu Ala Phe Val Val Asp Lys Asn Leu Arg His Arg Ser Ser Tyr Phe Phe Leu Asn Leu Ala Ile Ser Asp Phe Phe Val Gly Val Ile Ser Ile Pro Leu Tyr Ile Pro His Thr Leu Phe Glu Trp Asp Phe Gly Lys Glu Ile Cys Val Phe Trp Leu Thr Thr Asp Tyr Leu Leu Cys Thr Ala Ser Val Tyr Asn Ile Val Leu Ile Ser Tyr Asp Arg Tyr Leu Ser Val Ser Asn Ala Val Ser Tyr Arg Thr Gln His Thr Gly Val Leu Lys Ile Val Thr Leu Met Val Ala Val Trp Val Leu Ala Phe Leu Val Asn Gly Pro Met Ile Leu Val Ser Glu Ser Trp Lys Asp Glu Gly Ser Glu Cys Glu Pro Gly Phe Phe Ser Glu Trp Tyr Ile Leu Ala Ile Thr Ser Phe Leu Glu Phe Val Ile Pro Val Ile Leu Val Ala Tyr Phe Asn Met Asn Ile Tyr Trp Ser Leu Trp Lys Arg Asp His Leu Ser Arg Cys Gln Ser His Pro Gly Leu Thr Ala Val Ser Ser Asn Ile Cys Gly His Ser Phe Arg Gly Arg Leu Ser Ser Arg Arg Ser Leu Ser Ala Ser Thr Glu Val Pro Ala Ser Phe His Ser Glu Arg Gln Arg Arg Lys Ser Ser Leu Met Phe Ser Ser Arg Thr Lys Met Asn Ser Asn Thr Ile Ala Ser Lys Met Gly Ser Phe Ser Gln Ser Asp Ser Val Ala Leu His Gln Arg Glu His Val Glu Leu Leu Arg Ala Arg Arg Leu Ala Lys Ser Leu Ala Ile Leu Leu Gly Val Phe Ala Val Cys Trp Ala Pro Tyr Ser Leu Phe Thr Ile Val Leu Ser Phe Tyr Ser Ser Ala Thr Gly Pro Lys Ser Val Trp Tyr Arg Ile Ala Phe Trp Leu Gln Trp Phe Asn Ser Phe Val Asn Pro Leu Leu Tyr Pro Leu Cys His Lys Arg Phe Gln Lys Ala Phe Leu Lys Ile Phe Cys Ile Lys Lys Gln Pro Leu Pro Ser Gln His Ser Arg Ser Val Ser Ser

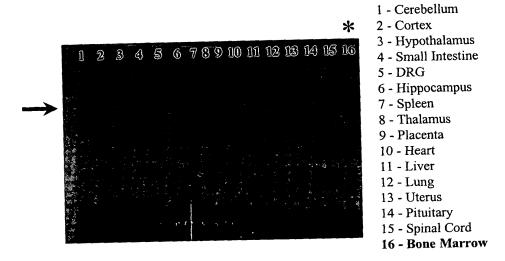
Docket No.: PRD-0034

App No.: Not Yet Assigned Filed: Herewith
Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE
Inventors: Lovenberg et al.

Attorney: Felicity E. Groth Sheet 3 of 13

Phone: (215) 568-3100

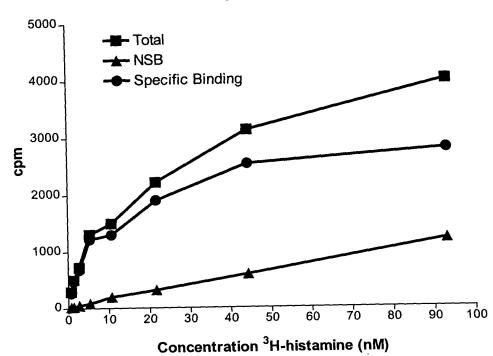
Figure 3: Tissue Distribution of human histamine H4 receptor



4/13

Figure 4: Binding of [3H]-histamine to pH4R expressing COS7 cells.

Binding of ³H-histamine to pH4R-transfected COS7 cells



Docket No.: PRD-0034 App No.: Not Yet Assigned

App No.: Not Yet Assigned Filed: Herewith
Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE

Inventors: Lovenberg et al. Attorney: Felicity E. Groth Sheet 5 of 13

h Phone: (215) 568-3100

5/13

FIGURE 5A

Mouse H4 DNA coding region (SEQ.ID.NO.:5)

ATGTCGGAGTCTAACAGTACTGGCATCTTGCCACCAGCTGCTCAGGTCCCCTTGGCATTTTTAATGT CTTCATTTGCCTTTGCTATAATGGTAGGCAATGCTGTGGTCATCTTAGCCTTTGTGGTGGACAGAAA CCTTAGACATCGAAGTAATTATTTTTTTTTTAATTTGGCTATTTCTGACTTCCTCGTGGGTTTGATT TCCATTCCTCTGTACATCCCTCACGTGTTGTTTAACTGGAATTTTGGAAGTGGAATCTGCATGTTTT GGCTCATTACTGACTATCTTTTGTGCACCGCATCTGTCTACAATATTGTCCTCATTAGCTACGATCG ATACCAGTCAGTTTCAAATGCTGTGTCTTATAGGGCTCAACACACTGGCATCATGAAGATTGTTGCT CAAATGGTGGCTGTTTGGATACTGGCTTTCTTGGTAAATGGCCCGATGATTCTTGGCTTCAGATTCTT GGAAGACAGCACGAACACAAAGGACTGTGAGCCTGGCTTTGTTACAGAGTGGTACATCCTCACCAT TACAATGCTCTTGGAATTCCTGCTTCCTGTCATCTCTGTGGCTTATTTCAATGTACAGATTTACTGG AGCCTGTGGAAGCGTAGGGCTCTCAGTAGGTGCCCTAGCCATGCTGGATTCTCCACTACCTCTTCCA GTGCTTCAGGACACTTACACAGAGCTGGGGTGGCTTGCAGGACAAGTAATCCTGGATTGAAGGAATC AGCTGCATCTCGTCACTCAGAAAGTCCTCGAAGAAAGACCAGCATCCTGGTGTCCTTAAGGACTCAC ATGAACAGCAGTATCACTGCCTTCAAAGTGGGTTCCTTCTGGCGATCGGAAAGTGCAGCGCTTCGCC AAAGGGAGTACGCAGAGCTTCTCAGAGGCAGGAAGCTAGCCAGGTCACTGGCCATCCTTCTGAGCGC TTTTGCCATTTGCTGGGCTCCATACTGTCTGTTCACAATTGTCCTTTCAACTTACCCCAGAACGGAA CGCCCAAATCGGTGTGGTACAGCATTGCCTTCTGGCTGCAATGGTTCAATTCGTTTGTTAATCCCT TTCTGTACCCTTTGTGTCACAGGCGTTTCCAGAAGGCTTTCTGGAAGATACTTTGTGTGACAAAGCA ACCAGCGCTGTCACAGAACCAGTCAGTATCTTCTTGA

Docket No.: PRD-0034
App No.: Not Yet Assigned Filed: Herewith
Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE
Inventors: Lovenberg et al.

Attorney: Felicity E. Groth Sheet 6 of 13

Phone: (215) 568-3100

6/13

FIGURE 5B

Rat H4 DNA coding region (SEQ.ID.NO.:6)

CCTTAGACATCGAAGTAATTATTTTTTTTTTAATTTGGCTATTTCTGACTTCTTCGTGGGTGTCATC ${\tt TCCATTCCTCTGTACATCCCTCACACGCTGTTTAACTGGAATTTTGGAAGTGGAATCTGCATGTTTT$ GGCTCATTACTGACTATCTTTTGTGCACAGCATCCGTCTACAGTATTGTCCTCATTAGCTACGATCG ATACCAGTCAGTTTCAAACGCTGTGCGTTATAGAGCACAGCACACTGGCATCCTGAAAATTGTTGCT \ CAAATGGTGGCTGTTTGGATACTGGCTTTCTTGGTCAATGGCCCAATGATTCTTGGCTTCGGATTCTT GGAAGAACACCAACACAGAGGAGTGCGAGCCTGGCTTTGTTACTGAGTGGTACATCCTCGCCAT TACAGCATTCTTGGAATTCCTGCTCCCTGTCTCCTTGGTGGTCTATTTCAGTGTACAGATTTACTGG AGCCTGTGGAAGCGTGGGAGTCTCAGTAGGTGCCCTAGCCACGCTGGATTCATCGCTACCTCTTCCA GGGGCACTGGACACTCACGCAGAACTGGGTTGGCTTGTAGGACAAGTCTTCCTGGATTAAAGGAACC AGCCGCATCCCTTCATTCAGAAAGTCCACGAGGAAAGAGCAGTCTCCTGGTGTCCTTAAGGACTCAC ATGAGCGGTAGTATCATCGCCTTCAAAGTGGGTTCCTTCTGCCGATCAGAAAGCCCAGTGCTTCACC AGAGAGAGCACGTGGAGCTTCTCAGAGGCAGGAAGCTAGCCAGGTCGCTAGCTGTCCTCCTGAGTGC TTTTGCCATTTGCTGGGCTCCGTATTGCCTGTTCACAATTGTTCTTTCAACTTATCGCAGAGGGGAG $\tt CGCCCCAAATCGATTTGGTACAGCATAGCCTTTTGGCTACAGTGGTTCAATTCACTTATTAATCCCT$ TTCTATACCCTTTGTGCCACAGACGTTTCCAGAAGGCTTTCTGGAAGATACTCTGTGTGACAAAGCA ACCAGCACCTTCACAGACCCAGTCAGTATCTTCTTGA

Docket No.: PRD-0034 App No.: Not Yet Assigned Filed: Herewith Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE Inventors: Lovenberg et al. Phone: (215) 568-3100

Attorney: Felicity E. Groth Sheet 7 of 13

7/13

FIGURE 5C

Guinea Pig H4 DNA coding sequence (SEQ.ID.NO.:7)

ATGTTGGCAAATAACAGTACAATCGCCTTAACATCAATTAAAATTTCTTTGACATTTTTA ATGTCTTTACTAGCTATTGCTATAATGTTAGGCAATGTCGTGGTCATTTTAGCTTTTATTG TGGACAGAAATCTTAGACATCGAAGTAATTACTTTTTTCTTAACTTGGCCATTGCAGACT TCTTTGTGGGTGCAATTGCAATTCCTCTGTACATACCTTCCTCGCTGACTTACTGGACTT CTGGAAAGCAAGCTTGTGTATTTTGGCTCATTACTGACTATCTTTTATGtACAGCATCTGT TAGAGCTCAGCACTCTGGCACCTGGAAAATTGCTACTCAGATGGTGGCTGTTTGGATAT TCTCCTTCATGACAAATGGGCCGATGATTCTGATTTCAGACTCTTGGCAGAATAGCACT ACAGAATGTGAACCTGGATTTTTAAAAAAGTGGTACTTTGCTCTCCCTACATCATTATTG GAATTCCTGATCCCCATCTTGTTAGTTGCTTATTTCAGCGCCCATATTTACTGGAGCCTG TGGAAGCGAGAAACTGAGCAGGTGCCTCAGCCACCCTGTACTCCCCTCTGACTCTTC CAGCAGTGACCACGGACACTCCTGCAGACAGGACCCCGATTCAAGGGCGACTCTGCCA GCACGGAAAGAACAACTGCCTCTCTTGGTTCAGACAAGTCACGGAGAAAGAGCAGTC TCTTGTTTTCCATAAGAGCCTACAAGAACAGCAATGTGATCGCTTCCAAAATGGGCTTC CTCTCCCACTCAGATTCCCTGGCTCTTCAGCAAAGGGAACATATCGAACTTTTCAGAGC CAGGAAATTAGCCAAGTCACTGGCCATACTCTTAGCAGCTTTTGCCATTTGCTGGGCTCC ATATTCACTGACTACAGTTATCTACTCATTTTTTCCTGAAAGGAACTTGACTAAATCAAC CTGGTACCATACTGCCTTTTGGCTCCAGTGGTTCAATTCCTTTGTTAATCCCTTTTTTGTAT CCATTGTGTCACAAACGTTTTCAGAAGGCTTTCCTGAAAATACTTCCTGTGAGAAGGCA ATCCACGCCACCACACACCGCTCAATATCCACTTGA

Docket No.: PRD-0034

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Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE
Inventors: Lovenberg et al.
Attorney: Felicity E. Groth Phone: (215) 568-3100

Sheet 8 of 13

Phone: (215) 568-3100

8/13

FIGURE 6A

Mouse histamine H4 receptor protein sequence (SEQ.IN.NO.:8)

MSESNSTGILPPAAQVPLAFLMSSFAFAIMVGNAVVILAFVVDRNLRHRSNYFFLNLAISDFL VGLISIPLYIPHVLFNWNFGSGICMFWLITDYLLCTASVYNIVLISYDRYQSVSNAVSYRAQH TGIMKIVAQMVAVWILAFLVNGPMILASDSWKNSTNTKDCEPGFVTEWYILTITMLLEFLLP VISVAYFNVQIYWSLWKRRALSRCPSHAGFSTTSSSASGHLHRAGVACRTSNPGLKESAASR HSESPRRKSSILVSLRTHMNSSITAFKVGSFWRSESAALRQREYAELLRGRKLARSLAILLSA FAICWAPYCLFTIVLSTYPRTERPKSVWYSIAFWLQWFNSFVNPFLYPLCHRRFQKAFWKIL CVTKQPALSQNQSVSS

Docket No.: PRD-0034

App No.: Not Yet Assigned Filed: Herewith
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Inventors: Lovenberg et al.

Attorney: Felicity E. Groth

Sheet 9 of 13

Phone: (215) 568-3100

9/13

FIGURE 6B

Rat histamine H4 receptor protein sequence (SEQ.ID.NO.:9)

MSESNGTDVLPLTAQVPLAFLMSLLAFAITIGNAVVILAFVADRNLRHRSNYFFLNLAISDFF VGVISIPLYIPHTLFNWNFGSGICMFWLITDYLLCTASVYSIVLISYDRYQSVSNAVRYRAQH TGILKIVAQMVAVWILAFLVNGPMILASDSWKNSTNTEECEPGFVTEWYILAITAFLEFLLPV ${\tt SLVVYFSVQIYWSLWKRGSLSRCPSHAGFIATSSRGTGHSRRTGLACRTSLPGLKEPAASLH}$ SESPRGKSSLLVSLRTHMSGSIIAFKVGSFCRSESPVLHQREHVELLRGRKLARSLAVLLSAFAICWAPYCLFTIVLSTYRRGERPKSIWYSIAFWLQWFNSLINPFLYPLCHRRFQKAFWKILCV TKQPAPSQTQSVSS

Docket No.: PRD-0034
App No.: Not Yet Assigned
Filed: Herewith
Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE
Inventors: Lovenberg et al.

Attorney: Felicity E. Groth Sheet 10 of 13 Phone: (215) 568-3100

10/13

FIGURE 6C

Guinea Pig histamine H4 receptor protein sequence (389 amino acids) (SEQ.ID.NO.:10)

MLANNSTIALTSIKISLTFLMSLLAIAIMLGNVVVILAFIVDRNLRHRSNYFFLNLAIADFFVG
AIAIPLYIPSSLTYWTSGKQACVFWLITDYLLCTASVYNIVLISYDRYQSVSNAVWYRAQHS
GTWKIATQMVAVWIFSFMTNGPMILISDSWQNSTTECEPGFLKKWYFALPTSLLEFLIPILLV
AYFSAHIYWSLWKREKLSRCLSHPVLPSDSSSSDHGHSCRQDPDSRATLPARKETTASLGSD
KSRRKSSLLFSIRAYKNSNVIASKMGFLSHSDSLALQQREHIELFRARKLAKSLAILLAAFAIC
WAPYSLTTVIYSFFPERNLTKSTWYHTAFWLQWFNSFVNPFLYPLCHKRFQKAFLKILPVRR
QSTPPHNRSIST

Docket No.: PRD-0034 App No.: Not Yet Assigned Filed: Herewith Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE Inventors: Lovenberg et al. Attomey: Felicity E. Groth Sheet 11 of 13

4)	Sheet 11 of			Phone. (213)	300-3100			
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), M	120 1117 120 120	240 237 240 240	360	480 477 480 480	594 591 600 600	711 711 711 717 717	831 831 837 837	951 951 957
Nucleotide Sequence Comparison of Human (SEQ ID NO:1), Guinea Pig (SEQ ID NO:7), Mouse (SEQ ID NO:5), and Rat H4 (SEQ ID NO:6)	Human: ATGCCAGATACTAATAGCACACAATTATCACTAAGCACTCGTGTTACTTTAGCATTTTTATGCTTAGTAGCTTTTGCTATAATGCTAGGAAATGCTTTGGTCATTTAGCTTTTAGCTTTT Guinea Pig: ATGTTGGCAAATAACAGTACAATCGCCTTAACATCAATTAAAATTTCTTTGACATTTTTAATGTTAGCTATTAGTTATAGGCAATGTTGGGTCATTTAGCTTTT Mouse: ATGTCGGAGTCTAACAGTACTGGCATCTTGCCACGTGCTCAGGTCCCCTTGGCATTTTTTAATGCTTTGCCTTTGCCTATAATGGTAGGCAATGCTGTGGTCATTTAGCCTTT Rat: ATGTCGGAGTCTAACGGCACTGACGTCTTGCCACTGCTCCTAGGCATTTTTAATGTCCCTGCTTGCT	Human: GTGGTGGACAAAAACCTTAGACATGGAAGTAATTTTTTTT	Human: GATTTTGGAAAGGAATCTGTGTATTTTGGCTCACTACTGACTATCTGTTATGTACAGCATCTGTATAACATTGTCCTCATCAGCTATGATCGATACCTGTCAGTCTAAATGCTGTG Guinea Pig: ACTTCTGGAAAGCAAGCTTGTGTATTTGGCTCATTACTGACTATCTTTTAGGCACAGCATCTGTGTATAATTGTCCTCATCAGCTACGATCGGTACCAGTCAGT	TCTTATAGAACTCAACATACTGGGGTCTTGAAGATTGTTACTCTGATGGTGGCGCGTTTGGGTGCTGGCCTTCTTAGTGAATGGGCCAATGATTCTAGTTTCAGAGTCTTGGAAGGATGAA TGGTATAGAGCTCAGCACTCTGGCACCTGGAAAATTGCTACTCAGATGGTGGCTGTTTGGATATTCTCCTTCATGAAAAGGGCCGATGATTCTGAATTCTGGAAAATAGC TCTTATAGGGCTCAACACACTGGCATCATGAAGATTGTTGCTCAAATGGTGGCTGTTTGGATACTGGCTTTCTTGGTAAATGGCCCGATGATTCTGGGTTCTTGGAAGAACAGC CGTTATAGAGCACAGCAC	Human: GGTAGTGAAIGIGAACCIGGATITITITCGGAAIGGTACAICCITGCCAITCTITCIGGAAITCGGAGAICCITAGITGATCGTTAITTCAACAIGAAGAIGTTAC Guinea Pig: ACTACAGAAIGIGAACCIGGAITITITAAAAAAGIGGIACTITGCICICCCIACAITAITGGAAITICCIGAICCCCAICTIGITAGITGGITGAITAITICAAIGIAATAITITAC Mouse: ACGAACACAAAAGGAIGIGAGCIGGCITIGITACAGAGIGGIACAICCICACCAITACAAGCAITCITGGAAITCCIGCTICCIGICGIGGIGGIGGITAITICAGIGAACAGAITIAC Rat: ACCAACACAGAGAGIGGGAGCCIGGCITIGITACIGAGIGGIACAICCICGCCAITACAGCAITCITGGAAITCIGGAAITCCCIGCICCITGITGITAITACAGIGIAACAGAITIAC	: TGGAGCCTGTGGAAGCGTGATCATCTCAGTAGGTGCCAAAGCCATCCTGGACTGACTGCTGTCTTTCCAACATCTGTGGACACTCATTCAGAGGTAGACTATCTTCAAGGGAGATCT : TGGAGCCTGTGGAAGCGAGAGAAACTGAGTAGCTGCCCTCAGCCCCCTCTCACTTTCCAGCAGTGACTACCTCTGCAGACGAGAGCTTGCAGAGACGTAGCCTGTGGAGGCTTGCAGGACCTGCCTG	 CTTCTGCATCGACAGAAGTTCCTGCATCCTTTCATTCAGAGAGAG	TCCTTCTCCCAATCAGATTCTGTAGCTCTTCACCAAAGGGAACATGTTGAACTGCTTAGAGCCAGGAGATTAGCCAAGTCACTGGCCATTCTCTTAGGGGTTTTTGCTGGTGCTTTGCTGGGGCT TTCCTCTCCCCACTCAGATTCCCTGGCTCTTCAGCAAAGGGAACATATCGAACTTTTCAGAGCCAGGAAATTAGCCAAGTCACTGGCCATACTCTTAGCAAAGGGGCTTTTGCTGGGGCT TCCTTCTGGCGATCGGAAAGTGCAGCGCTTCGCCAAAGGGAGTACGCAGAGGCTAGGCAGGAAGCTAGCCAGGTCACTGGGCCATCCTTCTGAGGGCTTTTGCTGGGGCT
	Huma Guinea Pi Mous Ra	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:	Human: Guinea Pig: Mouse: Rat:

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Inventors: Lovenberg et al.
Attorney: Felicity E. Groth Phone: (215) 568-3100
Sheet 12 of 13

117	1 Part・ サACCTTTTCTACACACACACACACACACACACACACACAC	Ted
117	Mouse: TACCCTTTGTGTCACAGGGGTTTCCAGAAGGCTTTCTGGAAGATACTTTGTGTGACAAGCAAG	Mouse
117	Guinea Pig: TATCCATTGTGTCACAAACGTTTTCAGAAGGCTTTTCCTGAAAATACTTCCTGTGAGAAGGCAATCCACGCCACCACACAACGGCTCAATATCCACTGA	Guinea Pig
117	Human: TATCCATTGTGTCACAAGGGGTTTCTTGAAAATATTTTGTATAAAAAGCAACCTCTACCATCACAACAGGGTGGGT	Нишап
107	Rat: CCGTAITIGCCTGTICACAATTGTTCTTTTCAACTTAICGCAGAGGGGGGGGGCCCCCAAATCGATTTGGTACAGCATAGCCTTTTGGCTACAGTGGTTCAATTCACTTATTAATCCCTTTCTA 107	Rat
107	Mouse: CCATACTGTCTGTTGACAATTGTCCTTTGAACTTACCCCAGAAAGGGCCCCAAATCGGTGTGGTAGCACTACACTTTGGCTGCAATGGTTCAATTGTTTAATCCTTTATTG 107	Mouse
101	Guinea Pig: CCATATTCACTGACTACTGTTATCTTACTTGATTATGGAACTTGACTAAATCAACCTGGTACCATACTGCCTTTTGGCTCCAGTGGTTCATTGTTAATCCCTTTTTG 107	Guinea Pig
2	Human: CCATATTCTCTGTTCACATTGTCCTTTCATTTTATTCCTCAGCAACAGGTCCTAAATCAGTTTGGTATAGAATTGCTTTTGGCTTCAGTGGTTCAATTCCTTTTGTCAATTCTCTTTTG 10/	Human

Docket No.: PRD-0034 App No.: Not Yet Assigned Filed: Herewith Title: DNAs ENCODING MAMMALIAN HISTAMINE RECEPTOR OF THE H4 SUBTYPE Inventors: Lovenberg et al. Attomey: Felicity E. Groth Sheet 13 of 13

Figure 8	ino Acid sequence Comparison of Human (SEQ ID NO:2), Guinea Pig (SEQ ID NO:10),	Mouse (SEQ ID NO:8) and Rat H4 (SEQ ID NO:9)
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	100 99 100 100	198 197 200 200	297 299 299	390 389 391 391
Mouse (SEQ ID NO:8) and Rat H4 (SEQ ID NO:9)	Human: MPDTNSTINLSLSTRVTLAFFMSLVAFAIMLGNALVILAFVVDKNLRHRSSYFFLNLAISDFFVGVISIPLYIPHTLFEWDFGKEICVFWLTTDYLLCTA Guinea Pig: MLANNSTIALT-SIKISLTFLMSLLAIAIMLGNVVVILAFIVDRNLRHRSNYFFLNLAIADFFVGAIAIPLYIPSSLTYWTSGKQACVFWLITDYLLCTA Mouse: MSESNSTGILPPAAQVPLAFLMSSFAFAIMVGNAVVILAFVVDRNLRHRSNYFFLNLAISDFLVGLISIPLYIPHVLFNWNFGSGICMFWLITDYLLCTA Rat: MSESNGTDVLPLTAQVPLAFLMSLAFAITIGNAVVILAF**D**NLRHRSNYFFLNLAISDFFVGVISIPLYIPHTLFNWNFGSGICMFWLITDYLLCTA CONSENSUS: MN.T .L: :::LF**MSL**AIM**GN.**VILAF**D**NLRHRS**XFFINLAI**DF**VG**I**IPLXIP**:L W. G : C:FWL**IDYLLCTA TM3 TM3	Human: SVYNIVLISYDRYLSVSNAVSYRTQHTGVLKIVTLMVAVWVLAFLVNGPMILVSESWKDEG-S-ECEPGFFSEWYILAITSFLEFVIPVILVAYFNMNIY Guinea Pig: SVYNIVLISYDRYQSVSNAVWYRAQHSGTWKIATQMVAVWIESFMTNGPMILISDSWQNST-T-ECEPGFLKKWYFALPTSLLEFLIPILLVAYFSAHIY Mouse: SVYNIVLISYDRYQSVSNAVSYRAQHTGIMKIVAQMVAVWILAFLVNGPMILASDSWKNSTNTECEPGFVTEWYILTITMLLEFLLPVISVAYFNVQIY Rat: SVYSIVLISYDRYQSVSNAVRYRAQHTGILKIVAQMVAVWILAFL:NGPMILSSSWKNSTNTEECEPGFVTEWYILAITAFLEFILPVSLVVYFSVQIY Consensus: SVXNIVLISYDRY SVSNAV YR:QH:G. KI MVAVW:::F:.NGPMIL:S:SW:::CEPGF:WY::::T.:LEF::P::.VAYF:IX TMA TMA	Human: WSLWKRDHLSRCQSHPGL-TAVSSNICGHSFRGRLSSRRSLSASTEVPASFHSERQRRKSSLMFSSRTKMNSNTIASKMGFESQSDSVALHQREHVELLR Guinea Pig: WSLWKREKLSRCLSHPVLPSDSSSSDHGHSCRQDPDSRATLPARKETTASLGSDKSRRKSSLLFSIRAYKNSNVIASKMGFLSHSDSLALQOREHIELFR Mouse: WSLWKRRALSRCPSHAGF-STTSSSASGHLHRAGVACRTSNPGLKESAASRHSESPRRKSSILVSLRTHMNSSITAFKVGSFWRSESAALRQREYAELLR Rat: WSLWKRGSLSRCPSHAGF-IATSSRGTGHSRRTGLACRTSLPGLKEPAASLHSESPRGKSSLLVSLRTHMSGSIIAFKVGSFCRSESPVLHQIEHVELLR Consensus: WSLWKR:.LSRC SH. : .: SS. GH. R .:R :::EAS: S:: R.KSSL::S R:A.K:G :::S:S::L:Q E::EL:R	Human: ARRLAKSLAILLGVFAVCWAPYSLFTIVLSFYSSATGPKSVWYRIAFWLQWFNSFVNPLLYPLCHKRFQKAFLKIFCIKKQPLPSQHSRSVSS Guinea Pig: ARKLAKSLAILLAAFAICWAPYSLTTVIYSFFPERNLTKSTWYHTAFWLQWFNSFVNPFLYPLCHKRFQKAFLKILPVRROSTPP-HNRSIST Mouse: GRKLARSLAILLSAFAICWAPYCLFTIVLSTYPRTERPKSVWYSIAFWLQWFNSFVNPFLYPLCHRRFQKAFWKILCVTKQPALSQ-NQSVSS Rat: GRKLARSLAVLLSAFAICWAPYCLFTIVLSTYRGERPKSIWYSIAFWLQWFNSLINPFLYPLCHRRFQKAFWKILCVTKQPAPSQ-TQSVSS Consensus: .R:LA:SLA:LL:FA:CWAPY:L T:: S ::KS.WY:.AFWLQWFNS::NP:LYPLCH:RFQKAF.KI: :::Q: .: .RS:S: TM6